fractures. Considering the nearly equal risk of secondary surgical procedures and the modest benefit in functional outcome, should we abandon the use of total hip arthroplasty in the treatment of hip fractures? Even if the benefits seem smaller than we previously thought, patients with high physical demands and a long remaining life expectancy should probably still be considered for treatment with total hip arthroplasty. Yet the expected remaining lifetime of those patients who potentially could benefit most from a total hip arthroplasty is much longer than the 2-year follow-up period used in the HEALTH trial. However, the number of secondary procedures after hemiarthroplasty may increase with longer follow-up. Therefore, one hopes that the HEALTH investigators will be able to provide long-term results from their trial in the future. Such data would be an even more important contribution to the knowledge base that supports hip-fracture treatment. There is still a need for large randomized, controlled trials or registry-based randomized clinical trials with greater numbers of patients in order to identify how factors such as patient activity level, biologic age, and remaining life expectancy influence the risk of secondary surgical procedures and functional outcome after hemiarthroplasty and total hip arthroplasty. Until then, in light of the results of the trial by Bhandari et al., we should probably be restrictive in the selection criteria for total hip arthroplasty for patients with hip fractures.

Disclosure forms provided by the author are available with the full text of this editorial at NEJM.org.

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Parting the Clouds over Typhoid with a New Conjugate Vaccine

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Typhoid fever is caused by fecal–oral transmission of *Salmonella enterica* serovar Typhi (*S.* Typhi). It has been a deadly companion to mankind for centuries, affecting 10.9 million persons and resulting in an estimated 116,800 deaths per year.[1] Although vaccines against typhoid have been available for more than a century and have been shown to be protective,[2,3] the approved vaccines (injectable Vi polysaccharide and oral, live-attenuated Ty21a typhoid vaccines) have not been useful in populations with a high typhoid burden, particularly in young children.[4] To address this shortfall, the Bill and Melinda Gates Foundation, as well as other donors, has supported the development of new typhoid conjugate vaccines (TCVs), generated data on disease burden, and coordinated with international stakeholders to introduce the vaccine in countries where typhoid fever is endemic.

Typbar-TCV was developed by Bharat Biotech International in India and was prequalified by the World Health Organization (WHO)[3] on the basis of immunogenicity and evidence of protection (55% efficacy) in a typhoid human challenge model.[5] In this issue of the *Journal*, Shakya et al.[6] report that this vaccine was immunogenic and efficacious against blood culture–confirmed ty-

phoid fever, with an estimated vaccine efficacy of 81.6% at 12 months, in a trial involving children who were between 9 months and 16 years of age.

Data from African and Asian surveillance studies were used by the WHO Strategic Advisory Group of Experts to recommend the use of TCVs in countries where typhoid fever is endemic.[2,4] Subsequently, TCVs were added to vaccines subsidized by Gavi, the Vaccine Alliance. The Typbar-TCV vaccine is already commercially available in India. Other large studies, such as the TCV introduction program in Navi Mumbai, India (ClinicalTrials.gov number, NCT03554213), are currently ongoing,[7] and introduction of the vaccine through Gavi subsidies in Asian and African countries is also under way. Ongoing and planned clinical trials are geared toward systematic assessment of vaccine performance and addressing unanswered scientific questions regarding effectiveness, herd immunity, cost-effectiveness, and the effect of the vaccine on antimicrobial resistance. The trial by Shakya and colleagues, combined with evidence of safety and immunogenicity in other trials,[7] provides support for broader introduction of TCVs in countries where typhoid is endemic. The national and international stakeholders involved in decisions regarding the introduction of TCV await results from longer-term follow-up to determine whether protection elicited by TCVs exceeds that of existing Vi polysaccharide and live-attenuated oral vaccines.

Typhoid fever has been successfully treated with antimicrobial agents since early in the antimicrobial era, but sustained antibiotic pressure through large-scale (over)use has created multidrug-resistant and extensively drug-resistant (XDR) typhoid strains that have spread in India, Bangladesh, and Pakistan.[8] Patients with severe *S.* Typhi infection caused by a resistant strain often have prolonged hospital stays and limited treatment options. Moreover, the presenting signs and symptoms of typhoid fever are nonspecific, and diagnostic testing is hampered by the poor sensitivity and limited availability of existing tests, including blood cultures (which, although insensitive, are considered to be the best available test for typhoid fever), particularly in resource-limited areas. Thus, patients with suspected typhoid fever in areas where typhoid is endemic frequently receive antimicrobial agents from health care providers, and unnecessary antimicrobial pressure is added to resident bacterial populations. To date, XDR typhoid is confined to India, Bangladesh, and Pakistan, where newer antibiotics are available.[8] Yet, it is easy to envision that the introduction of XDR *S.* Typhi strains into Africa, with underresourced health care systems and a lack of treatment options, could lead to a scenario involving considerable morbidity and mortality.

Additional large-scale trials are under way to provide data on vaccine performance in other geographic areas. The Typhoid Vaccine Acceleration Consortium (TyVAC) is evaluating TCV in Dhaka, Bangladesh (in a cluster-randomized trial), Blantyre, Malawi (in an individually randomized trial), and Ouagadougou, Burkina Faso (in coadministration studies).[9] Researchers in the THECA (Effect of a Novel Typhoid Conjugate Vaccine in Africa: A Multicenter Study in Ghana and the Democratic Republic of the Congo) trial are in close alignment with the TyVAC, conducting a cluster-randomized trial in Agogo, Ghana, and a large-scale trial of vaccine effectiveness in Kisantu, Democratic Republic of Congo.[10] This compendium of data for stakeholders in the introduction of vaccine may be used to target interventions to protect as many persons as possible given the existing constraints on resources.

Shakya and colleagues have made an important contribution to the global fight against *S.* Typhi infection, but global health is about impact. If further studies support and extend these results, how can a corresponding reduction in the burden of typhoid disease and death be achieved most efficiently?

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